REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the claims. Claims 73, 77, 82, 86-101, and 122 have been canceled without prejudice of disclaimer. Claims 72, 75, 78-81 and 83-85 have been amended. Claims 123-128 are newly presented. After entry of the amendment, claims 72, 74-76, 78-81, 83-85, 102-121 and 123-128 will be pending. Claims 102-121 have been withdrawn by the Examiner as drawn to a non-elected invention.

Applicants submit the amendment is supported throughout the specification, including for example at page 5, lines 5-18 and page 96, lines 25-31 , and does not introduce new matter.

Information Disclosure Statement

A copy of Lin et al., cited on the IDS filed November 30, 2007, is enclosed herewith. Applicants respectfully request consideration of the reference.

Claim Objection

Claim 88 was objected to as containing as informality. Claim 88 has been canceled without prejudice or disclaimer. The objection is therefore moot.

Written Description

Claims 72-83, 85-99, 101, and 122 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

Without acquiescing to the rejection and solely for advancing prosecution of the present application, claims 73, 77, 82, 86-99, 101, and 122 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in a continuation application. The rejection is addressed insofar as it applies to claims 72, 74-76, 78-81, 83, and 85.

The Office Action alleges the specification does not adequately describe a genus of molecules having at least 80% identity with the amino acid sequence of SEQ ID NO:X. Applicants respectfully do not agree.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP § 2163(I) (emphasis added). An Applicant may show possession of an invention by disclosure of sufficiently detailed, relevant identifying characteristics (i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between structure and function, or some combination of such characteristics) that provide evidence that Applicant was in possession of the claimed invention. *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964 (Fed. Cir. 2002); MPEP § 2163(II)(3)(A)(a). An actual reduction to practice, however, is not required for written description. *Falkner v. Inglis*, No. 05-1324, slip. op. at 13 (Fed. Cir. May 26, 2006).

The written description requirement must be applied in the context of the particular invention and state of the knowledge. *Capon v. Eschar*, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005). It is unnecessary to spell out every detail of the invention in the specification. Only enough must be included to convince a person of skill in the art that the inventor possessed the invention. *Falkner v. Inglis*, No. 05-1234, slip. op. at 14 (Fed Cir. May 26, 2006) (citing *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.,* 424 F.3d 1336, 1345 Fed. Cir. 2005).

Applying these standards, Applicants submit the specification sufficiently describes the genus of Bv8 and EV-VEGF recited in the amended claims.

With respect to Bv8, the claims have been amended to recite that Bv8 comprises at least 80% amino acid identity with SEQ ID:2 or SEQ ID NO:4. The specification discloses Bv8 variants having at least 80% amino acid sequence identity to SEQ ID NO:2 and SEQ ID NO:4. Both the long and short forms of human, mouse, and rat Bv8 were known. See, for example, Wecheselberger et al., 1999, *FEBS Lett.*, 462:177-81; Li et al., 2001, *Mol. Pharmacol.*, 59:692-698; and Masuda et al., 2002, *Biochem. Biophys. Res. Commun.*, 293(1), 396-402. As shown below, the short form contains an internal deletion that eliminates a heparin-binding domain.

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                                                                .:..*******:
Human L   AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGKLGDSCHPLTRKNNFGNGRQERRKR
Mouse L   AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGQVGDSCHPLTRKSHVANGRQERRRA
Rat L     AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGQVGDSCHPLTRKSHVANGRQERRRA
Human S   AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGKLGDSCHPLTRK------------
Mouse S   AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGQVGDSCHPLTRK------------
Rat S     AVITGACDKDSQCGGGMCCAVSIWVKSIRICTPMGQVGDSCHPLTRK------------
          ***********************************::**********


          ** *****
Human L   KRSKRKKEVPFFGRRMHHTCPCLPGLACLRTSFNRFICLAQK
Mouse L   KRRKRKKEVPFWGRRMHHTCPCLPGLACLRTSFNRFICLARK
Rat L     KRRKRKKEVPFWGRRMHHTCPCLPGLACLRTSFNRFICLARK
Human S   --------VPFFGRRMHHTCPCLPGLACLRTSFNRFICLAQK
Mouse S   --------VPFWGRRMHHTCPCLPGLACLRTSFNRFICLARK
Rat S     --------VPFWGRRMHHTCPCLPGLACLRTSFNRFICLARK
                  ***:*****************************:*
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Species	Form	% ID to SEQ ID NO:2	Reference
Human	Long (L)		SEQ ID NO:2
Mouse	Long (L)	89	FIG. 7 in specification
Rat	Long (L)	89	Masuda et al., 2002, Biochem. Biophys. Res. Commun., 293(1), 396-402 (GenBank Acc. No. NP_001032630)
Human	Short (S)	79	SEQ ID NO:4
Mouse	Short (S)	75	FIG. 6 in specification
Rat	Short (S)	75	Masuda et al., 2002, Biochem. Biophys. Res. Commun., 293(1), 396-402 (GenBank Acc. No. NP_620207)

SEQ ID NO:2 has 89% identity to the long form of mouse Bv8 and rat Bv8, 79% identity to the short form of human Bv8, and 75% identity to the short form of mouse Bv8 and rat Bv8, Outside of the heparin binding domain, the short and long forms of human, mouse, and rat Bv8 only differ by 4 amino acids and have 10 conserved cysteines. Within the 21 amino acid heparin binding domain of the long forms of human, mouse, and rat Bv8, 14 of the 21 amino acids are identical. The human, rat, and mouse Bv8 also share at least one common function: the ability to induce contraction of gastrointestinal smooth muscle tissue. See, for example, Li et al., 2001, *Mol. Pharmacol.*, 59:692-698.

In addition, conserved structural features among Bv8 from different species such as human, rat mouse, snake, and frog were known. A characteristic feature of the family of Bv8 proteins is the N-terminal AVIT sequence and the 10 Cys with identical spacing in the C-terminal domain. See, for example Kaser et al., 2003, *EMBO Reports*, 4:469-473. The N-terminal AVIT sequence was known to be necessary for biological activity. For example, deletion of the AVIT sequence was known to result in Bv8 variants that were able to bind to prokineticin receptors but unable to activate the receptors. See Negri et al., 2005, *Brit. J. Pharmacol.*, 146:625-632. Therefore, conserved structural features necessary for preserving biological activity of Bv8 were known.

In view of the demonstrated structural and functional similarities between human, mouse, frog, snake, and rat Bv8, the conserved structural features of the AVIT protein family, and the knowledge and high level of skill in the art, one of ordinary skill in the art would have recognized that Applicants were in possession of the genus of Bv8 polypeptides recited in the amended claims.

With respect to EG-VEGF, the claims have been amended to recite that EG-VEGF comprises at least 90% amino acid identity with SEQ ID NO:8 or amino acids 20-105 of SEQ ID NO:8. Human, rat, mouse, and bovine EG-VEGF sequences were known. See the amino acid sequence alignment of identified EG-VEGF species in Table 1. Human EG-VEGF was known to have approximately 91% amino acid identity to rat EG-VEGF and approximately 88% amino acid identity to mouse and bovine EG-VEGF, including 10 conserved Cys with identical spacing in the C-terminal domain. Human, rat, mouse, and bovine EG-VEGF were also known to share at least one common function: the ability to induce proliferation of endothelial cells. See, for example LeCouter et al., 2003, *Endocrinology*, 144:2606-2616; Masuda et al., *Biochem. Biophys. Res. Commun.*, 293:396-402; and Kisliouk et al., 2005, *Endocrinology*, 146:3950-3958.

Table 1

```
CLUSTAL W (1.8) multiple sequence alignment of EG-VEGF species

 HuEG-VEGF       AVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHPGSHKVPFFRKRKHHTCP
 RtEG-VEGF       AVITGACERDVQCGAGTCCAISLWLRGLRLCTPLGREGEECHPGSHKIPFFRKRQHHTCP
 BvEG-VEGF       AVITGACERDVQCRAGTCCAVSLWLRGLRVCTPLGRAGEECHPGSHKVPFFRKRQHHACP
 MsEG-VEGF       AVITGACERDIQCGAGTCCAISLWLRGLRLCTPLGREGEECHPGSHKIPFLRKRQHHTCP
                 **********:** ******:********:****** **********:**:***:**:**

 HuEG-VEGF       CLPNLLCSRFPDGRYRCSMDLKNINF
 RtEG-VEGF       CSPSLLCSRFPDGRYRCSQDLKNVNF
 BvEG-VEGF       CLPNLLCSRGLDGRYRCSTNLKNINF
 MuEG-VEGF       CSPSLLCSRFPDGRYRCFRDLKNANF
                 * *.*****  ******  :*** **
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	Species	% Identity to Mature Human EG-VEGF*	Reference
HuEG-VEGF	human	100	Specification at Figure 16A
RtEG-VEGF	rat	91	Masuda et al., 2002, *Biochem. Biopyhs. Res. Commun.*, 293:396-402.
BvEG-VEGF	bovine	88	Kisliouk et al., 2005, *Endocrinology*, 146:3950-3958.
MuEG-VEGF	mouse	88	LeCouter et al., 2003, *Endocrinology*, 144:2606-2616.

* Amino acid residues 20-105 of SEQ ID NO:2.

In addition, EG-VEGF was known to be a member of the AVIT protein family and shared conserved structural features with Bv8. A characteristic feature of the Bv8 polypeptides and the EG-VEGF polypeptides is the N-terminal AVIT sequence and the 10 Cys with identical spacing in the C-terminal domain. See, for example Kaser et al., 2003, *EMBO Reports*, 4:469-473.

In view of the demonstrated structural and functional similarities between human, mouse, rat, and bovine EG-VEGF, the conserved structural features of the AVIT protein family, and the knowledge and high level of skill in the art, one of ordinary skill in the art would have recognized that Applicants were in possession of the genus of EG-VEGF polypeptides recited in the amended claims.

Withdrawal of the written description rejection is respectfully requested.

Anticipation

1) Claims 72-76, 82-90, 98-101, and 122 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 7,264,801 (hereinafter the '801 patent). Applicants respectfully traverse this rejection.

Without acquiescing to the rejection and solely for the purpose of advancing prosecution, claims 73, 82, 86-90, 98-101, and 122 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in a continuation application. The rejection is addressed insofar as it applies to claims 72, 74-76, 83-85, and 123-128.

In order to anticipate a claim, the prior art reference must teach each and every element of the claim. *See* MPEP 2131.01, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The identical invention must be shown in the same complete detail as is recited by the claims. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Claim 72 as amended recites contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF, or a combination to induce proliferation of said cells. The Office Action alleges the '801 patent discloses contacting antigen presenting cells with EG-VEGF to induce proliferation of B cells and T cells to make anti EG-VEGF antibodies. The '801 patent does not disclose contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF or a combination thereof, as recited in claim 72 as amended. Nor does the '801 patent disclose that Bv8, EG-VEGF, or a combination of Bv8 and EG-VEGF is capable of inducing the proliferation of lymphoid lineage progenitor cells or progeny thereof. The '801 patent therefore does not disclose all the elements of the claims as amended.

Claims 123-128 recite administering Bv8, EG-VEGF, or a combination thereof to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy. The '801 patent does not disclose such a step. The '801 patent therefore does not disclose all the elements of the claims as amended.

Citing *Bristol-Myers Squibb Co. v. Ben Venue Labs Inc.*, 246 F.3d 1368 (Fed. Cir. 2001), the Office Action alleges the assertion of an intended outcome in Applicants' claims does not distinguish the claims over the '801 patent since the intended outcome language does not result in manipulative differences in the steps of the claims. Applicants respectfully do not agree.

A new use of a known process is patentable. See 35 U.S.C. § 101 and. In *Bristol-Myers*, the claims in the patent at issue and the prior art where both directed to the same purpose (e.g., treating cancer), whereas the claims in the present application are directed to a purpose that is different from that disclosed in the '801 patent.

The '801 patent teaches that EG-VEGF induces proliferation of endothelial cells and angiogenesis and that antagonists of EG-VEGF can inhibit endothelial cell proliferation and angiogenesis. In contrast, the specification discloses that Bv8, EG-VEGF, or a combination thereof induces hematopoiesis and can increase the population of T cells and B cells. Hematopoiesis is different from angiogenesis. The claims in the present application are therefore directed to a different purpose than that disclosed in the '801 patent and are patentable.

In view of the forgoing, Applicants submit the claims as amended are not anticipated by the '801 patent. Withdrawal of the rejection is respectfully requested.

2) Claims 72-81, 86-90, 93-97, and 122 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,485,938 (hereinafter the '938 patent). Applicants respectfully traverse this rejection.

Without acquiescing to the rejection and solely for the purpose of advancing prosecution, claims 73, 77, 86-90, 93-97, and 122 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in a continuation application. The rejection is addressed insofar as it applies to claims 72, 74-76, 78-81, and 123-128.

Claim 72 as amended recites contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF, or a combination thereof to induce proliferation of said cells. The '938 patent does not disclose contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF, or a combination thereof. Nor does the '938 patent disclose that Bv8, EG-VEGF, or a combination is capable of inducing the proliferation of lymphoid lineage progenitor

cells or progeny thereof. The '938 patent only provides evidence that Zven 1 is capable of inhibiting proliferation of lung carcinoma cells. See, for example, the '938 patent at Example 2. Therefore, the '938 patent does not teach or suggest all the elements of the claims as amended.

Claims 123-125 recite administering Bv8, EG-VEGF, or a combination thereof to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy to increase the population of T lymphocytes in the subject. Claims 126-128 recite administering Bv8 or a combination of Bv8 and EG-VEGF to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy to increase the population of white blood cells in the subject. The '938 patent does not disclose any of the steps of claims 123-128. Nor does the '938 patent disclose that Bv8, EG-VEGF, or a combination thereof is capable of increasing the population of T lymphocytes or white bloods cells in a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy. The '938 patent therefore does not disclose all the elements of the claims as amended.

The Office Action alleges the assertion of an intended outcome in Applicants' claims does not distinguish the claims over the '938 patent since the intended outcome language does not result in manipulative differences in the steps of the claims. Applicants respectfully do not agree.

As discussed above, a new use of a known method is patentable. The '938 patent does not disclose administering Zven 1 to induce the proliferation of lymphoid lineage progenitor cells or progeny thereof or administering Zven 1 to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy to increase the population of T lymphocytes or white blood cells in the subject. The claims in the present application are therefore directed to a different purpose than that disclosed in the '938 patent and are patentable.

In view of the forgoing, Applicants submit the claims as amended are not anticipated by the '938 patent. Withdrawal of the rejection is respectfully requested.

3) Claims 72-76, 82, 84-90, 98-101, and 122 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Application Publication 20030027998 (hereinafter the '998 publication). Applicants respectfully traverse this rejection.

Without acquiescing to the rejection and solely for the purpose of advancing prosecution, claims 73, 77, 82, 86-90, 98-97, and 122 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in a continuation application. The rejection is addressed insofar as it applies to claims 72, 74-76, and 84-85.

Claim 72 as amended recites contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF, or a combination thereof to induce proliferation of said cells. The '998 publication does not disclose contacting lymphoid lineage progenitor cells or progeny thereof with Bv8, EG-VEGF, or a combination thereof. Nor does the '998 publication disclose that Bv8, EG-VEGF, or a combination thereof is capable of inducing the proliferation of lymphoid lineage progenitor cells or progeny thereof. The '998 publication therefore does not disclose all the elements of the claim 72 as amended or any of the claims depending from claim 72.

Claims 123-125 recite administering Bv8, EG-VEGF, or a combination thereof to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy to increase the population of T lymphocytes in the subject. Claims 126-128 recite administering Bv8 or a combination of Bv8 and EG-VEGF to a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy to increase the population of white blood cells in the subject. The '998 patent does not disclose any of the steps of claims 123-128. The '998 patent also does not disclose does that Bv8, EG-VEGF, or a combination thereof is capable of increasing the population of T lymphocytes in a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy or that Bv8 or a combination of Bv8 and EG-VEGF is capable of increasing the population of white blood cells in a subject following treatment with an immunosuppressive agent, radiation, or chemotherapy. The '938 patent therefore does not disclose all the elements of the claims as amended.

In view of the forgoing, Applicants submit the claims as amended are not anticipated by the '998 patent. Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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